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REMARKS

Reconsideration is respectfully requested. Claims 13-17 remain in the application. Claim 18 has been canceled.

Informal Drawings

The Examiner has noted that the informality of the drawings, which are acceptable for examination purposes <u>only</u>. Formal drawings will be filed when the application is allowed.

Oath

The Examiner has called to the Applicant's attention that the Oath or Declaration is defective and is requiring a new Oath or Declaration in compliance with 37 CFR 1.67(a) identifying the application by application number and filing date. Enclosed please find the Declaration referred to in Applicant's Amendment After Final Action dated November 7, 2001 that was inadvertently omitted.

Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 13-18 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 being cancelled; therefore the rejections to Claim 18 – namely (cc) through (ii) are now moot. The Applicant has made a sincere effort to amend the claims or to address the rejections set forth by the Examiner.

More specifically, as regards the remaining rejections raised by the Examiner:

(a) Claims 13, 16, 17, and 18 are incomplete because there is no antecedent basis for "said protein".

Claims 13, 16, and 17 are amended to provide proper antecedent basis; Claim 18 is cancelled.

Rejections to Claim 13

(b) The recitation of "time series of quantum vibrations associated to its elongation" is vague and indefinite because there is no definition of the term in the application.

Said expression is replaced by "temporal sequence of quantum vibrations"; support of said expression may be found on page 6, lines 11-15 of the specification; the meaning of said expression is clear from the specification.

(c) The recitation of "minimizing the global harmonic ... frequencies surrounding said initial frequency" is vague, indefinite, and incomprehensible.

This rejection of the Examiner is sincerely believed to be incorrect. The rejected phrase is a circumlocution of the formula of page 10, lines 2-8 of the specification; as such it is correct and therefore not vague or indefinite.

(d) The recitation of "the two synchronized frequencies" is incomplete because the phrase has no antecedent basis.

Claim 13 is amended to take in account the rejection of the Examiner by reciting "the two resulting synchronized frequencies".

(e) The recitation of "said initial frequency" is incomplete because the phrase has no antecedent basis.

Claim 13 is amended to take in account the rejection of the Examiner by reciting "an initial proper frequency".

(f) The recitation of "transposing the resulting frequencies into the audible domain" is vague and indefinite because the term is not defined in the application.

The meaning of "transposing the resulting frequencies into the audible domain" has been slightly amended as follows: "audible domain" has been replaced by "field of audible frequencies" as it emerges clearly from the specification.

(g) The recitation of "the code relative ... their central value taken as an origin" is vague and indefinite.

Claim 13 is amended in view to taken in account the objection of the Examiner.

(h) The recitation of "central value" is incomplete because the phrase has no antecedent basis.

Claim 13 is amended to take in account the rejection of the Examiner.

(i) The recitation of "similar sequences of notes and signatures" is vague and indefinite because the instant application does not disclose how to distinguish similar sequences of notes and signatures from dissimilar sequences of notes and signatures.

The applicant respectfully disagrees with this rejection. Please note, in particular, Page 10, lines 19-22; page 11, line 5; and page 12, lines 2-12 of the specification. These passages clearly show how to distinguish similar sequences of notes and signatures from dissimilar sequences of notes and signatures. However, in view to better point out the invention "sequences" have been replaced by "series". Support may be found in the hereabove mentioned pages.

(j) The recitation of "musical periods" is vague and indefinite because the term is not defined.

We do not agree with the position of the Examiner; this expression is clearly defined by reference to scaling waves, see page 2, lines 1-3 of the specification. As a matter of fact, several methods exist to determine said musical periods; there are mentioned on page 10, line 19.

Moreover, for one skilled of the art the meaning of the musical period is: "the coherent segments that make up a melody"; roughly equivalent to a sentence in prose (see for instance, Oxford Advanced Learner's Dictionary of Current English, AS Hornby, and the following website: www.omnidisc.com/Music/Glossary.html).

"Scaling waves" may be explained as follows (see also Annex A unfortunately in French and Annex B in English): the periodicity which appears in the scaling waves attaining a given scale enables one to understand the presence of musical type relationships, i.e., consonance phenomenon occurring and developing in a rhythmic way in the process involved.

(k) The recitation of "rectifying first collectively, then individually" is vague and indefinite because the term is not defined.

Claim 13 is amended to take in account the rejection of the Examiner.

(1) The recitation of "adjustment of phrasing to measure" is vague and indefinite because the term is not defined.

"Phrasing" as defined in the Dictionary cited above means: "the way in which a musician divides a piece of music into phrases by pausing at suitable places." This definition is also found in the specification, page 13, lines 4-6.

The definition of measure as it also emerges from the same Dictionary: "one of the short sections of equal length that a piece of music is divided into". "Measure" means also

the single recurrence of each regular pattern in a meter, consisting of a strong first beat and subsidiary beats. See also website: www.omnidisc.com/Music/Glossary.html.

(m) The recitation of "using a keyboard featuring a 'one key play' device" is vague and indefinite because it is not understood what is meant by the phrase.

This notion is well known by those skilled in the art. Some information may be found on the following website:

www.phy.duke.edu/~kolene/physics/labs/sound.html.

"One key play" means to play one note of the melody stored in a memory with each press. It must also be pointed out that there is a patent describing said method: GB 2 091 470.

(n) The recitation of "tone quality" is vague and indefinite because the term is not defined.

A synonym of "tone quality" is "timbre". See Annex C. See also, page 14 of the specification.

(o) The recitation of "determining the tone quality ... harmonic structure of each" is vague and indefinite because the meaning of the passage is not understood.

Claim 13 is amended to take in account the rejection of the Examiner. Moreover, Annex C clearly explains the determination of tone quality.

(p) The recitation of "the protein" is incomplete because there is no antecedent basis for the term.

Claim 13 is amended to take in account the rejection of the Examiner.

Rejections to Claims 14-15

(q) The recitation of "using a properly adjusted instrument" is vague and indefinite. No sort of adjustment of instruments is taught in the application.

Claims 14 and 15 are amended to take in account the rejection of the Examiner.

(r) The recitation of "being associated to the following code" is vague and indefinite because the nature of the association is not disclosed.

Claim 14 is amended to take in account the rejection of the Examiner.

Even though it is not specifically defined in the specification, the term "tuned" is a well-known term for the man skilled in the art. "Tuning" may be found in the following website: www.sfu.ca/sonic-studio/handbook (see for instance tempered-tuning.htm or equal-temperament.htm). It is also noted that "tuned" is equivalent to "tempered scale" which is clearly defined in the specification and in the document cited on page 1, line 14 (Compterendus de l'Académie des Sciences, 1983, 297, 829).

(s) The recitation of "specific to the epigenetic stimulation of protein biosynthesis, according to the chromatic tempered scale" is vague, indefinite, and incomprehensible.

Claim 14 is amended to take in account the rejection of the Examiner.

(t) The recitation of "SeC" (Claims 14 and 15) is vague and indefinite because the term is undefined.

"SeC" means clearly selenocysteine (see Annex D).

(u) The recitation of "specific to the epigenetic inhibition ... chromatic tempered scale" is vague, indefinite, and incomprehensible.

Claim 15 has been amended to delete the rejected phrase.

(v) The recitation of "by symmertrization of the notes relatively to the central G within the chromatic tempered scale" is vague, indefinite, and incomprehensible.

Claim 15 has been amended to delete the rejected phrase. However, note that Annex E clearly explains the meaning of "central G", G being considered as the middle point.

Rejection of Claims 16 and 17

(w) The recitation of "further stabilizing said protein synthesis" is incomplete because there is no antecedent basis for the passage.

Claim 16 has been amended to take in account the rejection of the Examiner.

(x) The recitation of "using a proper colored light transposition" is vague and indefinite because the term is not defined. The application does not disclose how to distinguish a proper colored light transposition from an improper colored light transposition.

Claim 16 has been amended to take in account the rejection of the Examiner.

(y) The recitation of "the mature protein" is incomplete because there is no antecedent basis for the phrase.

Claim 16 has been amended to delete the rejected phrase.

(z) The recitation of "transposing the quantum vibrations ... denoting central values" is incomprehensible.

Claim 16 has been amended to take in account the rejection of the Examiner.

(aa) Claims 16 and 17 are improper multiple dependent claims because Claim 16 depends from both Claims 13 and 14 not in alternative.

Claim 16 has been amended to provide proper dependency.

(bb) The recitation of "spatial positions of the colors ... representation of said protein" is vague and indefinite and incomprehensible.

Claim 17 has been amended to take in account the rejection of the Examiner.

In view of the amendments to Claims 13-17 set forth above, as well as the explanations relating to other objected to phrases, it is believed that the claims as now amended clearly comply with 35 U.S.C. § 112, second paragraph, and that this rejection is now moot.

Rejections Under 35 U.S.C § 112, first paragraph

Claims 13-18 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims contain new matter. The Applicant does not point to basis in the application as filed for each of the limitations and each of the newly filed Claims 13-18. In particular, Applicant does not point to support for each one of the items listed in Items (a) – (ii) in the rejection hereinabove. Office Action of April 16, 2002 at page 6.

In response to this rejection, the Applicant has noted and addressed each of the specific rejections under Items (a) – (bb) in comments relating to the rejections under 35 U.S.C. § 112, second paragraph. A number of the rejections such as (a), (d), (e), (h), (p) and (y) were for lack of antecedent basis and have been corrected. Support for other phrases, such as (b), (c), (i), (j), (l) and (n) is clearly set forth. As noted in the Amendment After Rejection dated November 7,

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2002, Claims 13-18 prior to this Amendment are translations of the claims that were approved in the European Patent Office.

As Applicant does not believe that new matter has been added, attached to this Amendment is a "Claim Support Outline" showing where each part of the claim is supported in the specification. From this Claim Support Outline, it is apparent that no new matter has been added.

It is therefore respectfully submitted that the claims as amended do not contain new matter and such rejection is no longer pertinent.

Claims 13-18 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to able one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Each of the points mentioned in the rejection hereinabove (Items (a) – (ii)) is incorporated herein. The invention is not described in such a way that one skilled in the art could understand or practice the invention. Applicant's arguments (Paper No. 13, pages 10-11) are not convincing because the Applicant makes assertions regarding phrases and pauses in translation without providing clear evidence of such phrases and pauses. Office Action of April 16, 2002 at page 6.

The Examiner's reconsideration of this rejection is respectfully requested. Where there is a period, there is a phase. The existence of a phase in protein synthesis may be checked by comparison with the pauses in elongation as determined from accumulation of intermediate nascent chains of discrete sizes, which may be observed using gel electrophoresis such as in the work of S. Varenne et al. (J. Mol. Biol. 180, 549-576, 1984). In the example given in this paper on pFW 565 (E. Coli's outer membrane protein A), pauses may not only be seen to fit the musical "cadences" located as explained in patent application (note the average period of amino acids near the maximum amplitude, *i.e.*, maximum number of intermediate nascent chains).

The mere fact that phases follow a regular pattern, as seen on figure 2 in contradistinction with the predictions of codon usage (which postulate that codon-anticodon binding follows a trial-and-error procedure, wherefrom pauses would simply be statistically correlated with rare codons, yielding a chaotic-like behavior), is by itself evidence of a phase, already in the case of bacteria, with "some" undetermined mechanism to control it – for which inventor's theoretically

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grounded scaling waves do provide an explanation (the theoretical papers are quoted in application, p. 1 and p. 2).

A periodicity is clearly visible on polyribosomes (See *Declaration of Dr. Joel Sternheimer II dated October 26, 2001*, Annex A of Attachment A, figure 1 from B. Alberts et al., Molecular Biology of the Cell, Garland Publishing, New York and London, 3rd edition 1994, p. 238).

In view of the publications available discussing phrases and pauses, the Applicant's assertions would clearly enable one skilled in the art to practice the invention.

Rejection Under 35 U.S.C. 101

Claims 13-18 stand rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

This rejection is repeated for the reasons already of record (e.g., Office Action mailed May 25, 2001, pages 6-7). Applicant's arguments (Paper No. 13, pages 4-6) and the Rule 132 Declarations by Dr. Sternheimer filed January 31, 2002 are not convincing. Annexes 7, 8, and 9 to the Rule 132 Declaration (executed October 26, 2001) have been given no weight because they are not in the English language. Annex 10 is not mentioned in the Declaration so its significance is not known. None of the points of either Declaration establishes a phase or pattern of translation of specific MRNAs into the polypeptides in a regular or phased pattern. Office Action of April 16, 2002, page 6.

The Examiner is sincerely requested to please revisit the issue of utility in this application. The Examiner has stated that Dr. Sternheimer's Declaration is not convincing; however, Dr. Sternheimer has presented evidence regarding utility. While such evidence may not be exactly what the Examiner deems to give 100% utility, the Examiner is reminded of the Federal Circuit position on such utility expressed in case of *In Re Cortright*, 49 U.S.P.Q.2d 1464, 1469 (Fed. Cir. 1999) discussed in the earlier filed Amendment After Final.

In fact, the specification does teach utility of the method for epigenetic regulation of protein biosynthesis *in situ* in Examples 5 and 6 of the specification at pages 24-28. This is confirmed by the first Declaration of Dr. Sternheimer dated May 19, 1999 and earlier filed in this case. As further support for utility, the Applicant submits herewith experiments made by French

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Canadian pupils which were interested to carry out the claimed methods. The results of their experiments are exposed in Annex F1 (English translation of Annex F2 which is the original document). Said experiments had also been summed up in a poster (Annex G1 which is an English translation of Annex G2 which is the original document).

A study of the effects of exposing *Vibrio fischeri* to the proteodics of its Lux A and Lux B genes is also presented to show utility of the claimed method (Annex H).

In view of the overwhelming amount of evidence of utility, it is respectfully submitted that there is sufficient evidence to show utility.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

Ernest B. Lipscomb, III Registration No. 24,733

Customer No. 00826 ALSTON & BIRD LLP Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Charlotte Office (704) 444-1000 Fax Charlotte Office (704) 444-1111 CLT01/4557975v1

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on October 15, 2002.

Janet/FI Moore

Version with Markings to Show Changes Made:

In the Claims:

13. (Once Amended) A method for epigenetic regulation of protein biosynthesis *in situ* by scale resonance comprising:

- A. determining the amino acid sequence of <u>a</u> [said] protein, then the sequence of musical notes corresponding to said amino acid sequence, through decoding and transposition into sound of <u>temporal sequences</u> [time series] of quantum vibrations associated to its elongation, by operating as follows:
 - determining the proper frequency of each amino acid in its free state, (a) equal to its mass multiplied by the square of the speed of light in vacuum and divided by Planck's constant; then minimizing the global harmonic distance between all the possible pairs [couples] of amino acids as a function of their proportion in environing transfer RNA population to which said amino acids are bound, by setting the condition that the displacement of the initial proper frequency of the amino acid in its free state as earlier determined, towards its bound state value which results in the synchronized frequency, be smaller than half the difference between the two resulting synchronized frequencies surrounding an [said] initial proper frequency, then transposing the resulting frequencies into the field of audible frequencies [audible domain], thus providing a code which allows the stimulation of the biosynthesis of said protein, the code for inhibition being deduced from the preceding code by symmetrization of the logarithms of the said audible frequencies around their central view (relative to its inhibition being obtained through a symmetrization of the logarithms of the frequencies just obtained relatively to their central value taken as origin];
 - (b) determining the musical periods by spotting the most significant similar series [sequences] of notes and signatures which result in a melodically and harmonically coherent progression;
 - (c) determining the <u>individual</u> lengths of the notes by <u>adjusting the</u> [rectifying first collectively then individually the periods as determined in step (b) through an

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adjustment of] phrasing to <u>the</u> measure, <u>which operation can be performed using</u> [controlled using] a keyboard <u>equipped with</u> featuring a 'one key play' device;

- (d) determining the tone quality or timbre by comparing the repartition of notes of said amino acid sequence to what is observed in average on the whole of proteins, wherefrom deducing which harmonies are amplified and which are softened, then selecting the closest timbre in a palette of given ones [through the retroaction of the whole set of amino acids of the protein on the harmonic structure of each]; and
- B. playing said sequence of musical notes *in situ* to stimulate or inhibit said protein biosynthesis, either directly, or indirectly by using a recording on any proper support of the sequence of musical notes heretofore obtained.
- 14. (Once Amended) The method according to Claim 13, characterized in that the code which allows for the [by producing, using a properly adjusted instrument, a sequence of musical notes, said notes being associated to amino acids according to the following code, specific to the epigenetic] stimulation of the [protein] biosynthesis, of said protein according to Claim 1A(a) is [the chromatic tempered scale in ascending order]:

Gly = low A; Ala = C; Ser = E; Pro, Val, Thr, Cys = F; Leu, Ile, Asn, Asp = G; Gln, Lys, Glu, Met = A; His = B flat; Phe, SeC = B; Arg, Tyr = sharp C; Trp = sharp D[.]

where the notes are tuned following the tempered scale, with low A at 220Hz.

15. (Once Amended) The method according to Claim 13, characterized in that the code for inhibition of the [producing, using a properly adjusted instrument, a sequence of musical notes, said notes being associated to amino acids according to the following codes, specific to the epigenetic inhibition of protein biosynthesis and derived from the following code, specific to the epigenetic stimulation of protein] biosynthesis of said protein[,] according to Claim 1A(a), is [the chromatic tempered scale in ascending order:

Gly = low A; Ala = C; Ser = E; Pro, Val, Thr, Cys = F; Leu, Ile, Asn, Asp = G; Gln, Lys, Glu, Met = A; His = B flat; Phe, SeC = B; Arg, Tyr = sharp C; Trp = sharp D

by symmetrization of the notes relatively to the central G within the chromatic tempered scale, to yield in ascending order]:

as deduced from the code of Claim 14 by taking the notes of the chromatic tempered scale which are symmetrical to those of the code of Claim 14 with respect to the central G.

- 16. (Once Amended) The method according to [Claim 13 or] Claim 14, characterized in that:
 - (a) one determines the 3-tridimensional structure of said protein,
- (b) the result obtained at the end of Claim 14 is further stabilizing by the action of [said protein synthesis using a proper] colored light transpositions of grouped [obtained by transposing the] quantum vibrations arising from the spatial conformation of the protein issued from said elongation, the spatial positions of said colors being the same as those of the amino acids in a tridimensional spatial representation of said protein, and their frequencies given by a code derived from that Claim 14 [associated to the mature protein once spatially fold over itself, according to a code which is derived from that obtained at the end of step (a) of Claim 14 specific to the stimulation of its biosynthesis,] through the formula

$$\upsilon = \upsilon_{\circ, \circ} (\cosh)^{-1} (e^{(f/f_{\circ})^{Log \cosh i}})$$

where f, f_o are the musical frequencies and υ , υ _o the colored ones, with the indices of denoting the central values.

17. (Once Amended) The [A] method of [according] to Claim 16, wherein said central value v is the frequency of lemon yellow, wherefrom said code reads [characterized in that the spatial positions of the colors are those occupied by the amino acids in a three-dimensional spatial representation of said protein, the code being]

Gly = dark red; Ala = bright red; Ser = orange; Pro, Val Thr, Cys = ochre; Leu,

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Ile, Asn, Asp = lemon yellow; Gln, Glu, Lys, Met = green; His = emerald; Phe = blue; Arg, Tyr = indigo; Trp = purple.

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Claim Support Outline

- 13. (Once Amended) A method for epigenetic regulation of protein biosynthesis *in situ* by scale resonance comprising:
- A. determining the amino acid sequence of a protein, then the sequence of musical notes corresponding to said amino acid sequence, through decoding and transposition into sound of temporal sequences of quantum vibrations associated to its elongation, by operating as follows:
 - (a) determining the proper frequency of each amino acid in its free state, equal to its mass multiplied by the square of the speed of light in vacuum and divided by Planck's constant; then minimizing the global harmonic distance between all the possible pairs of amino acids as a function of their proportion in environing transfer RNA population to which said amino acids are bound, by setting the condition that the displacement of the initial proper frequency of the amino acid in its free state as earlier determined, towards its bound state value which results in the synchronized frequency, be smaller than half the difference between the two resulting synchronized frequencies surrounding an initial proper frequency, then transposing the resulting frequencies into the field of audible frequencies, thus providing a code which allows the stimulation of the biosynthesis of said protein, the code for inhibition being deduced from the preceding code by symmetrization of the logarithms of the said audible frequencies around their central view;
 - (b) determining the musical periods by spotting the most significant similar series of notes and signatures which result in a melodically and harmonically coherent progression;
 - (c) determining the individual lengths of the notes by adjusting the phrasing to the measure, which operation can be performed using a keyboard equipped with featuring a 'one key play' device;

Specification, Page 1, lines 6-10; page 8, lines 6-7

Page 6, lines 11-15; Page 8, lines 6-11

Page 9, line 29 – Page 10, line 18

Page 10, lines 2-8

Page 10, lines 19-22; Page 11, line 12 et seq.; page 12, lines 2-12

Page 12, line 30 – Page 13, line 6
Page 13, line 9. See also response to rejection (m).

(d) determining the tone quality or timbre by comparing the repartition of notes of said amino acid sequence to what is observed in average on the whole of proteins, wherefrom deducing which harmonies are amplified and which are softened, then selecting the closest timbre in a palette of given ones; and B. playing said sequence of musical notes in situ to stimulate or inhibit said protein biosynthesis, either directly, or indirectly by using a recording on any proper support of the sequence of musical notes heretofore obtained.	Page 14, lines 8-21; also note Annex C
14. (Once Amended) The method according to Claim 13, characterized in that the code which allows for the stimulation of the biosynthesis, of said protein according to Claim 1A(a) is: Gly = low A; Ala = C; Ser = E; Pro, Val, Thr, Cys = F; Leu, Ile, Asn, Asp = G; Gln, Lys, Glu, Met = A; His = B flat; Phe, SeC = B; Arg, Tyr = sharp C; Trp = sharp D	See original Claim 4. Page 8, line 18 – Page 9, line 2.
where the notes are tuned following the tempered scale, with low A at 220Hz.	Page 9, lines 17-22. See also response to rejection (r).
15. (Once Amended) The method according to Claim 13, characterized in that the code for inhibition of the biosynthesis of said protein according to Claim 1A(a), is: Trp = C; Arg, Tyr = D; Phe, SeC = E flat; His = E; Gln, Lys, Glu, Met = F; Leu, Ile, Asn, Asp = G; Pro, Val, Thr, Cys = A; Ser = B flat; Ala = sharp D; Gly = sharp F as deduced from the code of Claim 14 by taking the notes of the chromatic tempered scale which are symmetrical to those of the code of Claim 14 with respect to the central G.	See original Claim 5. Page 9, lines 3-13.
16. (Once Amended) The method according to Claim 14, characterized in that: (a) one determines the 3-tridimensional structure of said protein, (c) the result obtained at the end of Claim 14 is further stabilizing by the action of colored light transpositions of grouped quantum vibrations arising from the spatial conformation of the protein issued from said elongation, the	See original Claim 7. Page 15, line 17-24.

spatial positions of said colors being the same as those of the amino acids in a tridimensional spatial representation of said protein, and their frequencies given by a code derived from that Claim 14 through the formula $\upsilon = \upsilon_{\bullet,\bullet}(\cosh)^{-1}(e^{(f/f_{\bullet})^{Log}\cosh i})$	
where f, f ₀ are the musical frequencies and v , v_0 the colored ones, with the indices ° denoting the central values.	
17. (Once Amended) The method of to Claim 16, wherein said central value v is the frequency of lemon yellow,	See original Claim 8. Page 15, line 24 – Page 16, line 5.
wherefrom said code reads Gly = dark red; Ala = bright red; Ser = orange; Pro, Val Thr, Cys = ochre; Leu, Ile, Asn, Asp =	
lemon yellow; Gln, Glu, Lys, Met = green; His = emerald; Phe = blue; Arg, Tyr = indigo; Trp = purple.	